REMARKS

Claims 1-15 are pending in this application. Claims 16-24 are withdrawn. Claim 1 has been amended to replace the phrase "prepared by granulating" with the term "comprising", to replace "less" with "not more", and to delete the phrase "the microcapsule being". Claim 11 has been amended to correct the spelling of rezatriptan and cetirizine. Support for these amendments may be found in original claim 1 and in the specification, for example at paragraphs [0014] and [0016]. No new matter has been added by reason of this amendment.

I. Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-15 under 35 U.S.C. §103(a) as allegedly obvious over *Gowan* (US 5,876,759) in view of *Ohta* (EP 0914818 and *Guo* (US 2004/0068000). For the following reasons, Applicants respectfully request that the rejection be withdrawn.

Applicants respectfully submit that the cited references, either alone or in combination, do not support a *prima facie* case of obviousness because they fail to teach or suggest the presently claimed invention.

The claimed tablet rapidly disintegrates in the oral cavity and comprises at least two types of granules compressed together: (a) rapidly dispersing granules comprising a sugar alcohol or a saccharide or a mixture thereof having an average particle size less than about 30 microns, and a disintegrant, and (b) "taste-masked microcapsules containing at least one drug" prepared by encapsulating a wet milled, "granulated mass" comprising "at least one drug" and "at least one polymeric binder". The claimed wet milled granules are "hard, flexible, [and] less friable" and do not have the undesirable levels of "fines" which result from dry milling (present specification, paragraph [0015]). Thus, drug-containing particles prepared as claimed have quite different properties compared to drug-particles prepared by other methods such as dry milling, and would reasonably have quite different properties compared to particles prepared without granulation and/or wet milling.

Gowan describes a compressed, orally disintegrating dosage form prepared by dry-blending: (a) drug particles having a taste-masking coating; (b) a water-disintegratable, compressible carbohydrate; and (c) a binder. *Gowan* explains that "[t]he ingredients are dry blended and then compressed into a mass, preferably a wafer." (Col. 3, lines 2-5). Thus,

Gowan, discloses a tablet comprising at least three separate types of particles: taste-masked drug particles, a compressible carbohydrate, and a binder.

Gowan fails to teach or suggest the granulated, wet milled and microencapsulated particles comprising a drug and a binder, as in the claimed invention. Milling in general would be expected to reduce the particle size of the granulated drug/binder particles, and wet milling, as noted above, imparts particular properties to the resulting milled particles, as well as reducing the levels of "fines", all of which provides an "optimum size distribution", which thereby provides the "smooth creamy mouthfeel" for a palatable orally disintegrating dosage form.

Gowan also teaches away from the rapid releasing granules of the claimed invention. *Gowan* indicates that disintegration in the oral cavity is provided by the "water-disintegratable, compressible carbohydrate" (col. 3, line 1), which "facilitate the breakup of the dosage form" (col. 3, lines 18-19). Furthermore, *Gowan* fails to disclose any other component which facilitates disintegration, for example disintegrants known in the art such as crospovidone. Thus, *Gowan* teaches that disintegration can be provided by a "compressible carbohydrate", alone, rather than the claimed rapid releasing granules comprising the combination of ≤ 30 μm sugar alcohol or saccharide particles and a disintegrant.

Guo discloses a solid dosage form (i.e., a tablet) which contains a solid core having an active ingredient having an "unpleasant taste" and a compression coating covering the solid core which provides taste-masking. The dosage forms of *Guo* are clearly intended to be swallowed whole, as there is no indication in *Guo* that they are intended to disintegrate in the oral cavity, and the drug particles in the core are not individually taste-masked, as would be required for an orally disintegrating tablet containing a unpleasant tasting drug. The core can additionally contain other excipients such as fillers (e.g., lactose, microcrystalline cellulose, etc.), and disintegrants (e.g., croscarmellose sodium). (*Guo*, page 3, Example 1).

Thus, *Guo* also fails to disclose: (a) individually taste-masked particles prepared by wet milling a granulate comprising the combination of a drug and a binder; and (b) rapidly dispersing granules comprising the combination of ≤ 30 μm sugar alcohol or saccharide particles and a disintegrant. Furthermore, the dosage forms of *Guo* are quite different from the orally disintegrating tablets of *Gowan* and the claimed invention, because the dosage

forms of *Guo* are intended to be swallowed whole, without disintegrating in the oral cavity of the patient.

Ohta describes tablets comprising a single type of drug-containing granule, i.e., prepared by granulating together a sugar alcohol or saccharide, a drug, and a disintegrant, which are then compressed into a rapidly disintegrating tablet. Furthermore, the drug particles of *Ohta* are not microencapsulated or otherwise taste-masked, do not include a polymeric binder, and are not prepared with a wet milling process step. As noted above, wet milling the claimed combination of drug and binder provides drug-containing particles with particular physical properties which are optimal for incorporation into an orally disintegrating tablet dosage form.

Thus, none of the cited references, either individually or in combination, support *prima facie* obviousness. None of the applied references disclose a drug-containing particle comprising the combination of a drug and a binder, which is first granulated, then wet milled, and finally coated with a taste-masking coating. *Gowan* does not disclose taste-masked drug-containing particles prepared by granulation or wet milling process steps, and none of the drug particles in *Gowan* contain a binder (the binder is added to the taste-masked drug particles as a separate component prior to compression into a tablet). *Guo* does not disclose individually taste-masked drug particles (rather, the entire tablet of *Guo* is encased in a taste-masking compression coating). *Ohta* does not disclose taste-masking at all.

Furthermore, none of the applied references disclose tablets comprising the combination of (a) individually taste-masked drug-containing particles and (b) rapid releasing granules comprising the combination of ≤ 30 μm sugar alcohol or saccharide particles and a disintegrant. As discussed above, *Gowan* teaches away from rapidly releasing granules by employing a "compressible carbohydrate" component (i.e., which do not have the ≤ 30 μm particle size of the sugar alcohol or saccharide component of the claimed rapid releasing microgranules, or a disintegrant component). *Guo* fails to disclose individually taste-masked drug particles or rapid releasing granules, and simply describes tablet cores comprising the taste-masked drug and additional excipients including separate lactose and croscarmellose sodium particles (i.e., not combined into a single granulate particle). *Ohta* fails to describe taste-masked drug-containing particles, and *Ohta* only describes tablets prepared by

compressing a single type a particle containing both drug, sugar alcohol or saccharide, and disintegrant.

The Examiner suggests that one skilled in the art would have been motivated to combine the compressed dosage forms of *Gowan* with the sugar alcohol or saccharide granules of *Ohta* to provide a rapidly disintegrating tablet according to the presently claimed invention. The Examiner argues that the motivation for the combination would have come from the desire to reduce the undesirable taste or bitterness of the *Gowan* tablet and to provide a pleasant taste perception.

However, Applicants respectfully submit that one skilled in the art would not have been motivated to incorporate the sugar alcohol or saccharide particles of *Ohta* into the tablets of *Gowan* for the simple reason that in the tablets of *Gowan* the drug already is coated with taste-masking polymers, which "are released from the dosage form with no objectionable taste" (col. 3, lines 6-7). Thus, one skilled in the art would not look to another reference, such as *Ohta*, to solve a problem that *Gowan* expressly states does not exist.

Moreover, even if *Gowan* and *Ohta* were combined, such combination could proceed in many different ways – the most reasonable of which would not provide the claimed tablet. For instance, one reasonable combination of *Gowan* and *Ohta* would be, as the Examiner suggests, to simply add the sugar alcohol or saccharide of *Ohta* to the three-part compression dry-blend of *Gowan*. The resulting tablet would simply be a compressed dry-blend of either three or four components, depending upon whether the sugar alcohol or saccharide was pre-blended with one of the other three components of the dry-blend prior to the compression. In any event, the resultant tablet would not be a compressed blend of two types of granules, as in the claimed invention.

Moreover, without improper hindsight, there is no reasonable motivation to combine *Gowan*, *Ohta*, and *Guo* in the manner proposed by the Examiner, as the cited references themselves lack sufficient direction for their combination in the manner suggested by the Examiner. For example, one could as readily compression coat the compositions of *Ohta* to provide taste masking or replace the taste-masked drug particles of *Gowan* with the drug-containing particles of *Ohta*; neither of which combinations would provide the claimed invention.

In view of the foregoing, Applicants respectfully submit that the rejection of claims 1-

15 under 35 U.S.C §103 as allegedly obvious is improper, and therefore request that it be withdrawn.

Furthermore, Applicants respectfully submit that the withdrawn claims recite all of the limitations of the pending claims under examination. For example, independent claim 16 recites a method for preparing a tablet that disintegrates in the oral cavity, prepared by granulating, wet milling, and microencapsulating a pharmaceutically acceptable formulation comprising at least one drug; preparing rapidly dispersing microgranules comprising a sugar alcohol or saccharide having an average particle size of not less than 30 μm, and a disintegrant; and compressing the drug-containing particles and rapidly releasing granules to form a tablet from which not less than 60% of the drug dissolves in about 60 minutes. The remaining withdrawn claims all depend from claim 16, directly or indirectly, and thus include these limitations. Accordingly, the withdrawn claims should be rejoined.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-1283. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. 1.136(a)(3).

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Respectfully submitted,
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